

AMENDMENTS TO THE SPECIFICATION

The following is a marked-up version of the specification with the language that is underlined ("___") being added and the language that contains strikethrough ("—") or double bracket ("[[]]") being deleted:

In the BACKGROUND OF THE INVENTION section:

(paragraph starting at page 1, line 25)

The receptor-type tyrosine kinases are comprised of a large number of transmembrane receptors with diverse biological activity. Approximately ~~20~~ Approximately, 20 different subfamilies of receptor-type tyrosine kinases have been identified. One tyrosine kinase subfamily is comprised of EGFR, HER2, HER3, and HER4. Ligands of this subfamily of receptors include epithelial growth factor, TGF- α , amphiregulin, HB-EGF, betacellulin and heregulin. Another subfamily of these receptor-type tyrosine kinases is the insulin subfamily, which includes INS-R, IGF-IR, and IR-R. The PDGF subfamily includes the PDGF- α and β receptors, CSFIR, c-kit and FLK-II. The FLK family is comprised of the kinase insert domain receptor (KDR), fetal liver kinase-1 (FLK-1), fetal liver kinase-4 (FLK-4) and the fms-like tyrosine kinase-1 (flt-1) (Plowman et al., DN&P 7(6):334-339, 1994, which is hereby incorporated by reference).

In the SUMMARY OF THE INVENTION section:

(paragraph starting at page 7, line 4)

According to still a further aspect of the present invention is a composition comprising a compound of formula I further comprising a second compound selected from the group consisting of an estrogen receptor modulator, an androgen receptor modulator, a retinoid receptor modulator, a cytotoxic agent, an anti-proliferative agent, a tyrosine kinase inhibitor, an inhibitor of epidermal-derived growth factor, an inhibitor of fibroblast-derived growth factor, an inhibitor of platelet derived growth factor, an MMP inhibitor, an integrin blocker, interferon- α , interleukin-12, pentosan polysulfate, a cyclooxygenase inhibitor, carboxyamidotriazole, combretastatin A-4, squalamine, 6-O-chloroacetyl-carbonyl-fumagillol, thalidomide, angiostatin, ~~and~~-troponin-1, tamoxifen and raloxifene.

In the DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS section:

(paragraph starting at page 9, line 3)

wherein R₃ is selected from the group consisting of: _ H; alkyl; alkenyl; alkynyl; halogen; aryl; heteroaryl containing N, O, or S; the aryl and heteroaryl may be further

substituted with halogen, an alkyl, alkenyl, and alkynyl; NZ_1Z_2 , wherein Z_1 and Z_2 are independently selected from the group consisting of: H and alkyl; and $(CO)Y_x$, wherein Y is selected from the group consisting of: H, alkyl, alkenyl, alkynyl, aryl, heteroaryl containing N, O, or S, and the aryl and heteroaryl may be further substituted with halogen, alkyl, alkenyl, and alkynyl; and wherein R_4 is selected from the group consisting of: H and alkyl.

(paragraph starting at page 10, line 30)

Also included in the scope of the claims is a method of treating cancer which comprises administering a therapeutically effective amount of a compound of Formula I, Formula II, Formula III and Formula IV in combination with radiation therapy and/or in combination with a compound generally known for use in selected cancers and selected from the group consisting of an estrogen receptor modulator, an androgen receptor modulator, a retinoid receptor modulator, a cytotoxic agent and an antiproliferative agent. These and other aspects of the invention will be apparent from the teachings contained herein.

(paragraph starting at page 13, line 4)

As appreciated by those of skill in the art, "halo" or "halogen" as used herein is intended to include chloro, fluoro, bromo and iodo. The term "heterocycle" or "heterocyclyl" as used herein is intended to mean a 5- to 10-membered aromatic or nonaromatic heterocycle containing from 1 to 4 heteroatoms selected from the group consisting of O, N and S, and includes bicyclic groups. "Heterocyclyl" therefore includes the above mentioned heteroaryls, as well as dihydro and tetrahydro analogs thereof. Further examples of "heterocyclyl" include, but are not limited to the following: benzoimidazolyl, benzofuranyl, benzofurazanyl, benzopyrazolyl, benzotriazolyl, benzothiophenyl, benzoxazolyl, carbazolyl, carboliny, cinnoliny, furanyl, imidazolyl, indoliny, indolyl, indolaziny, indazolyl, isobenzofuranyl, isoindolyl, isoquinolyl, isothiazolyl, isoxazolyl, naphthpyridiny, oxadiazolyl, oxazolyl, oxazoline, isoxazoline, oxetanyl, pyranyl, pyraziny, pyrazolyl, pyridaziny, pyridopyridiny, pyridaziny, pyridyl, pyrimidyl, pyrroly, quinoliny, quinolyl, quinoxaliny, tetrahydropyranyl, tetrazolyl, tetrazolopyridyl, thiadiazolyl, thiazolyl, thienyl, triazolyl, azetidiny, 1,4-dioxanyl, hexahydroazepiny, piperaziny, piperidiny, pyrrolidiny, morpholiny, thiomorpholiny, dihydrobenzoimidazolyl, dihydrobenzofuranyl, dihydrobenzothiophenyl, dihydrobenzoxazolyl, dihydrofuranly, dihydroimidazolyl, dihydroindolyl, dihydroisooxazolyl, dihydroisothiazolyl, dihydrooxadiazolyl, dihydrooxazolyl, dihydropyraziny, dihydropyrazolyl, dihydropyridiny, dihydropyrimidiny, dihydropyrroly, dihydroquinoliny, dihydrotetrazolyl, dihydrothiadiazolyl, dihydrothiazolyl, dihydrothienyl, dihydrotriazolyl, dihydroazetidiny, methylenedioxybenzoyl, tetrahydrofuranly, and tetrahydrothienyl, and N-oxides thereof.

In the EXAMPLES section:

(paragraph starting at page 28, line 11)

Molecules with the potential target biological activity were analyzed in a validated *in silico* assay that is based on public domain National Cancer Institute *in vitro* anti-cancer data. The molecules are first decomposed to 110 descriptors using a proprietary CHEMSAS™ algorithm. This decomposition process results in a molecular data pattern of 110 variables that is then input into the *in silico* model. The output of the model is a prediction of the -Log(GI50) for the molecule(s) being analyzed against the specific cancer cell type in question, i.e., breast cancer or leukemia, etc. A specific *in silico* assay was also developed for the leukemia cell line (i.e., K562) that over expresses the abnormal protein tyrosine kinase found in Chronic Myelogenous Leukemia (CML). Results of the *in silico* assay for molecular Formulas II and III in a number of cancer cell types are summarized below in Table 1.